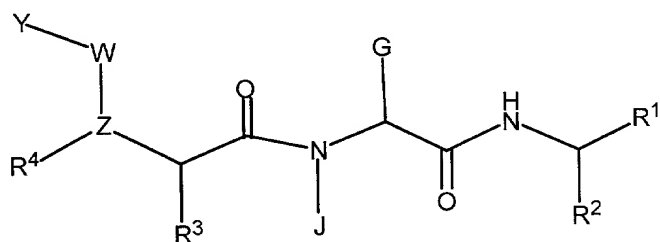


Claims

What is claimed is:

1. A compound, including enantiomers, stereoisomers, rotamers and tautomers of said compound, and pharmaceutically acceptable salts or solvates of said compound, said compound having the general structure shown in Formula I:



Formula I

wherein:

G, J and Y may be the same or different and are independently selected from the group consisting of the moieties: H, alkyl, alkyl-aryl, heteroalkyl, heteroaryl, aryl-heteroaryl, alkyl-heteroaryl, cycloalkyl, alkyloxy, alkyl-aryloxy, aryloxy, heteroaryloxy, heterocycloalkyloxy, cycloalkyloxy, alkylamino, arylamino, alkyl-aryl amino, arylamino, heteroaryl amino, cycloalkyl amino and heterocycloalkyl amino, with the proviso that Y may be additionally optionally substituted with X^{11} or X^{12} ;

X^{11} is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkyl-alkyl, heterocyclyl, heterocyclylalkyl, aryl, alkylaryl, arylalkyl, heteroaryl, alkylheteroaryl, or heteroarylalkyl moiety, with the proviso that X^{11} may be additionally optionally substituted with X^{12} ;

X^{12} is hydroxy, alkoxy, aryloxy, thio, alkylthio, arylthio, amino, alkylamino, arylamino, alkylsulfonyl, arylsulfonyl, alkylsulfonamido, arylsulfonamido, carboxy, carbalkoxy, carboxamido, alkoxycarbonylamino, alkoxycarbonyloxy, alkylureido, arylureido, halogen, cyano, or nitro, with the

proviso that said alkyl, alkoxy, and aryl may be additionally optionally substituted with moieties independently selected from X^{12} ;

R^1 is COR^5 or $B(OR)_2$, wherein R^5 is selected from the group consisting of H, OH, OR^8 , NR^9R^{10} , CF_3 , C_2F_5 , C_3F_7 , CF_2R^6 , R^6 and

- 5 COR^7 wherein R^7 is selected from the group consisting of H, OH, OR^8 , CHR^9R^{10} , and NR^9R^{10} , wherein R^6 , R^8 , R^9 and R^{10} may be the same or different and are independently selected from the group consisting of H, alkyl, aryl, heteroalkyl, heteroaryl, cycloalkyl, cycloalkyl, arylalkyl, heteroarylalkyl, $CH(R^1')COOR^{11}$, $CH(R^1')CONR^{12}R^{13}$, $CH(R^1')CONHCH(R^2')COOR^{11}$,
 10 $CH(R^1')CONHCH(R^2')CONR^{12}R^{13}$, $CH(R^1')CONHCH(R^2')R'$, $CH(R^1')CONHCH(R^2')CONHCH(R^3')COOR^{11}$, $CH(R^1')CONHCH(R^2')CONHCH(R^3')CONR^{12}R^{13}$, $CH(R^1')CONHCH(R^2')CONHCH(R^3')CONHCH(R^4')COOR^{11}$, $CH(R^1')CONHCH(R^2')CONHCH(R^3')CONHCH(R^4')CONR^{12}R^{13}$,
 15 $CH(R^1')CONHCH(R^2')CONHCH(R^3')CONHCH(R^4')CONHCH(R^5')COOR^{11}$, and $CH(R^1')CONHCH(R^2')CONHCH(R^3')CONHCH(R^4')CONHCH(R^5')CONR^{12}R^{13}$,
 wherein R^1' , R^2' , R^3' , R^4' , R^5' , R^{11} , R^{12} , R^{13} , and R' may be the same or different and are independently selected from a group consisting of H, alkyl,
 20 aryl, heteroalkyl, heteroaryl, cycloalkyl, alkyl-aryl, alkyl-heteroaryl, aryl-alkyl and heteroaralkyl;

Z is selected from O, N, or CH;

W maybe present or absent, and if W is present, W is selected from C=O, C=S, or SO_2 ; and

- 25 R, R' , R^2 , R^3 and R^4 are independently selected from the group consisting of H; C1-C10 alkyl; C2-C10 alkenyl; C3-C8 cycloalkyl; C3-C8 heterocycloalkyl, alkoxy, aryloxy, alkylthio, arylthio, amino, amido, ester,

carboxylic acid, carbamate, urea, ketone, aldehyde, cyano, nitro; oxygen, nitrogen, sulfur, or phosphorus atoms (with said oxygen, nitrogen, sulfur, or phosphorus atoms numbering zero to six); (cycloalkyl)alkyl and (heterocycloalkyl)alkyl, wherein said cycloalkyl is made of three to eight carbon atoms, and zero to six oxygen, nitrogen, sulfur, or phosphorus atoms, and said alkyl is of one to six carbon atoms; aryl; heteroaryl; alkyl-aryl; and alkyl-heteroaryl;

wherein said alkyl, heteroalkyl, alkenyl, heteroalkenyl, aryl, heteroaryl, cycloalkyl and heterocycloalkyl moieties may be optionally substituted, with said term "substituted" referring to optional and chemically-suitable substitution with one or more moieties selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, heterocyclic, halogen, hydroxy, thio, alkoxy, aryloxy, alkylthio, arylthio, amino, amido, ester, carboxylic acid, carbamate, urea, ketone, aldehyde, cyano, nitro, sulfonamide, sulfoxide, sulfone, sulfonylurea, hydrazide, and hydroxamate.

2. The compound of claim 1, wherein R^1 is COR^5 , and R^5 is H, OH, $COOR^8$ or $CONR^9R^{10}$.

3. The compound of claim 2, wherein R^1 is $COCONR^9R^{10}$, and R^9 is H, R^{10} is selected from the group consisting of H, $CH(R^{1'})COOR^{11}$, $CH(R^{1'})CONR^{12}R^{13}$, $CH(R^{1'})CONHCH(R^{2'})COOR^{11}$, $CH(R^{1'})CONHCH(R^{2'})CONR^{12}R^{13}$, and $CH(R^{1'})CONHCH(R^{2'})(R')$.

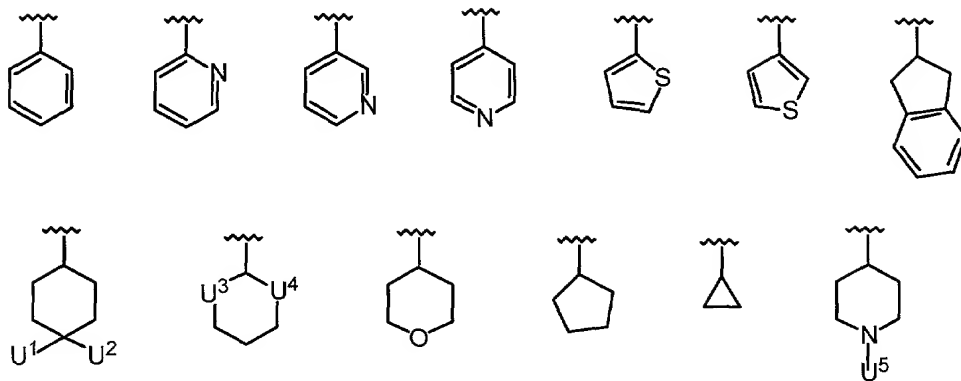
4. The compound of claim 3, wherein R^{10} is $CH(R^{1'})CONHCH(R^{2'})COOR^{11}$, $CH(R^{1'})CONHCH(R^{2'})CONR^{12}R^{13}$, or $CH(R^{1'})CONHCH(R^{2'})(R')$, wherein $R^{1'}$ is H or alkyl, heteroalkyl and $R^{2'}$ is phenyl, substituted phenyl, hetero atom-substituted phenyl, thiophenyl, cycloalkyl, piperidyl and pyridyl.

5. The compound of claim 4, wherein $R^{1'}$ is H.

6. The compound of claim 5, wherein R^{11} is H or *tert*-butyl;

R' is hydroxymethyl; and

R^{2'} is selected from the group consisting of:



5

wherein:

U¹ and U² maybe same or different and are independently selected from the group consisting of H, F, CH₂COOH, CH₂COOMe, CH₂CONH₂, CH₂CONHMe, CH₂CONMe₂, azido, amino, hydroxyl, substituted amino, substituted hydroxyl;

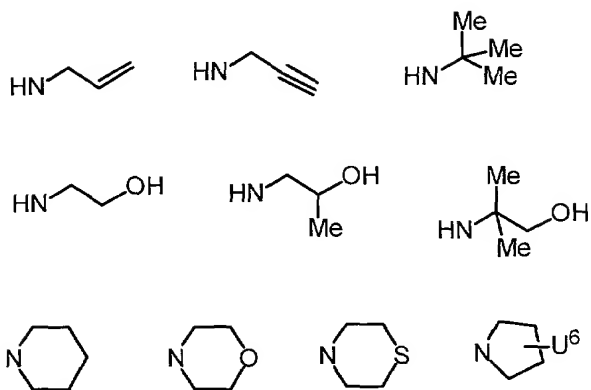
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U³ and U⁴ maybe same or different and are O or S;

15

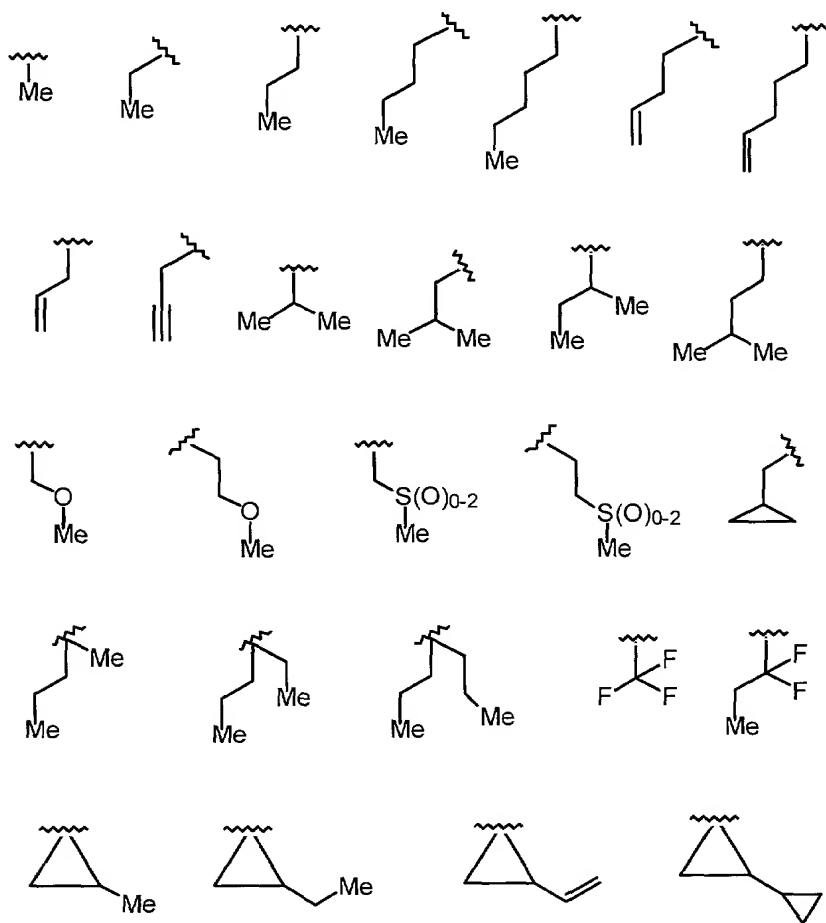
U⁵ is selected from the moieties consisting of alkylsulfonyl, aryl sulfonyl, heteroalkyl sulfonyl, heteroaryl sulfonyl, alkyl carbonyl, aryl carbonyl, heteroalkyl carbonyl, heteroaryl carbonyl, alkoxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylaminocarbonyl, arylaminocarbonyl and heteroarylamino carbonyl or combinations thereof; and

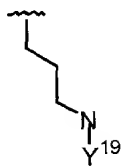
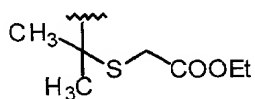
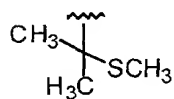
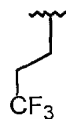
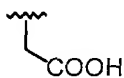
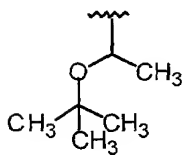
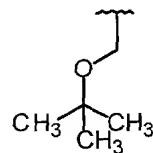
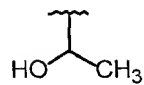
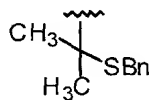
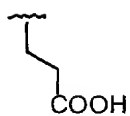
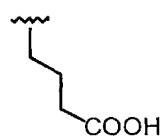
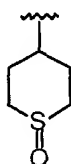
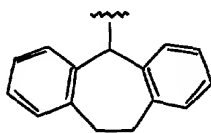
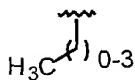
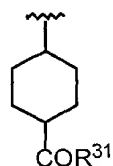
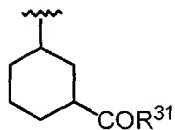
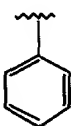
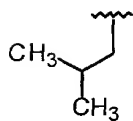
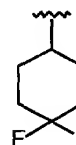
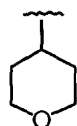
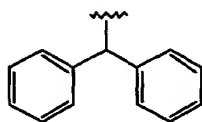
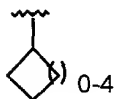
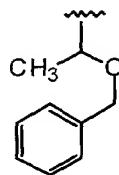
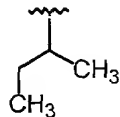
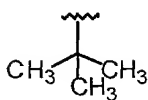
NR¹²R¹³ is selected from the group consisting of:

$\text{NH}_2, \text{NHMe}, \text{N(Me)OMe}, \text{NMe}_2,$ 

wherein U^6 is H, OH, or CH_2OH .

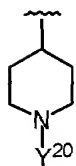
7. The compound of claim 2, wherein R^2 is selected from the group consisting of the following moieties:



CC(C)C

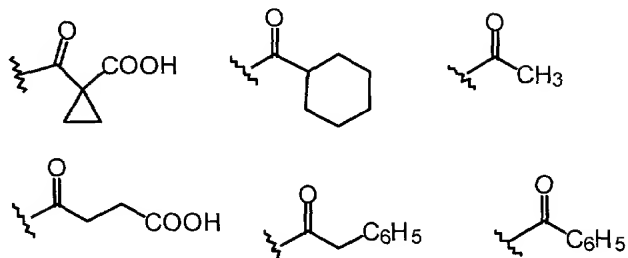
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and

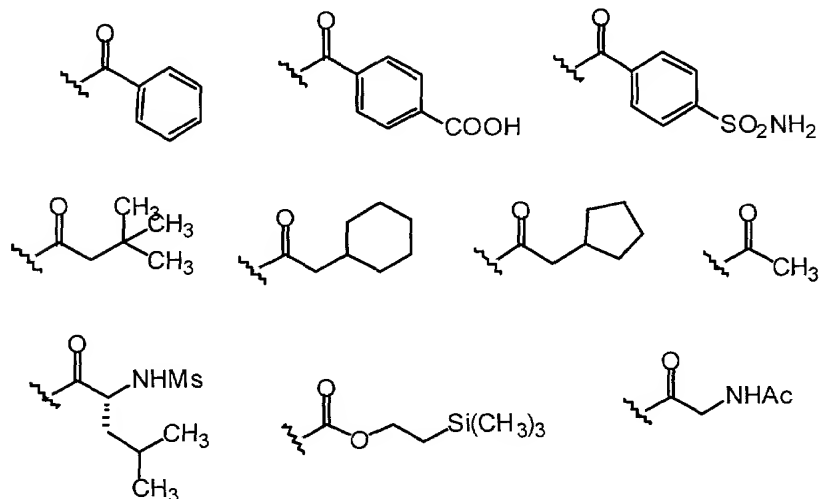


wherein $R^{31} = \text{OH}$ or O-alkyl;

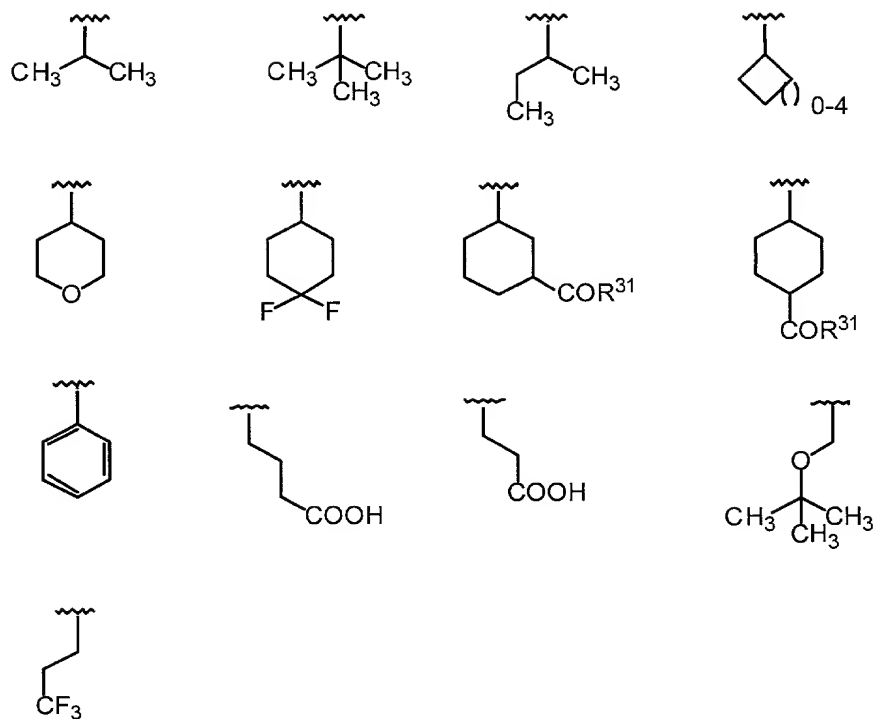
Y^{19} is selected from the following moieties:



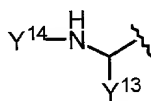
and Y^{20} is selected from the following moieties:

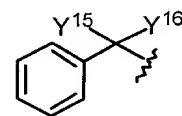
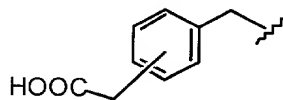
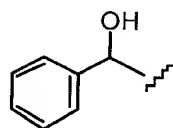
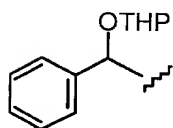
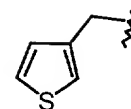
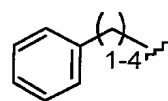
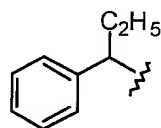
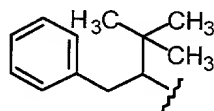
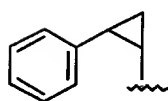
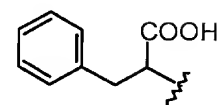
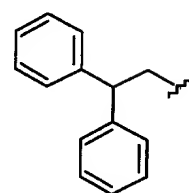
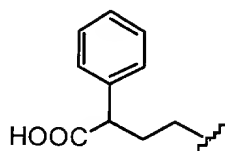
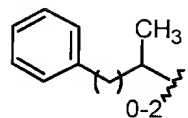
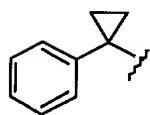
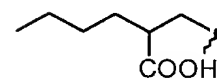
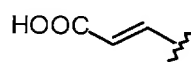
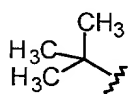
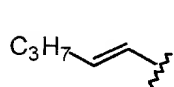
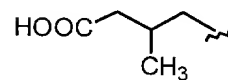
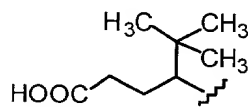
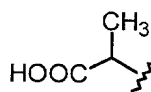
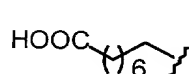
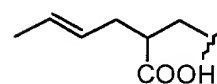
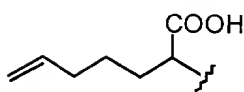
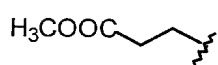
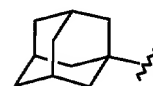
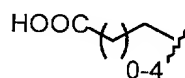
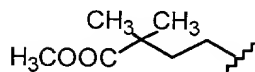
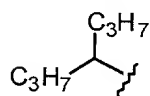
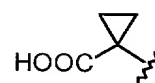
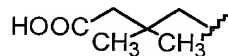
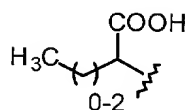
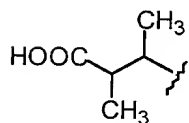
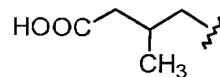
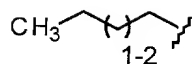
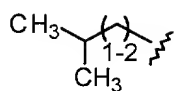
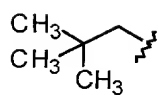


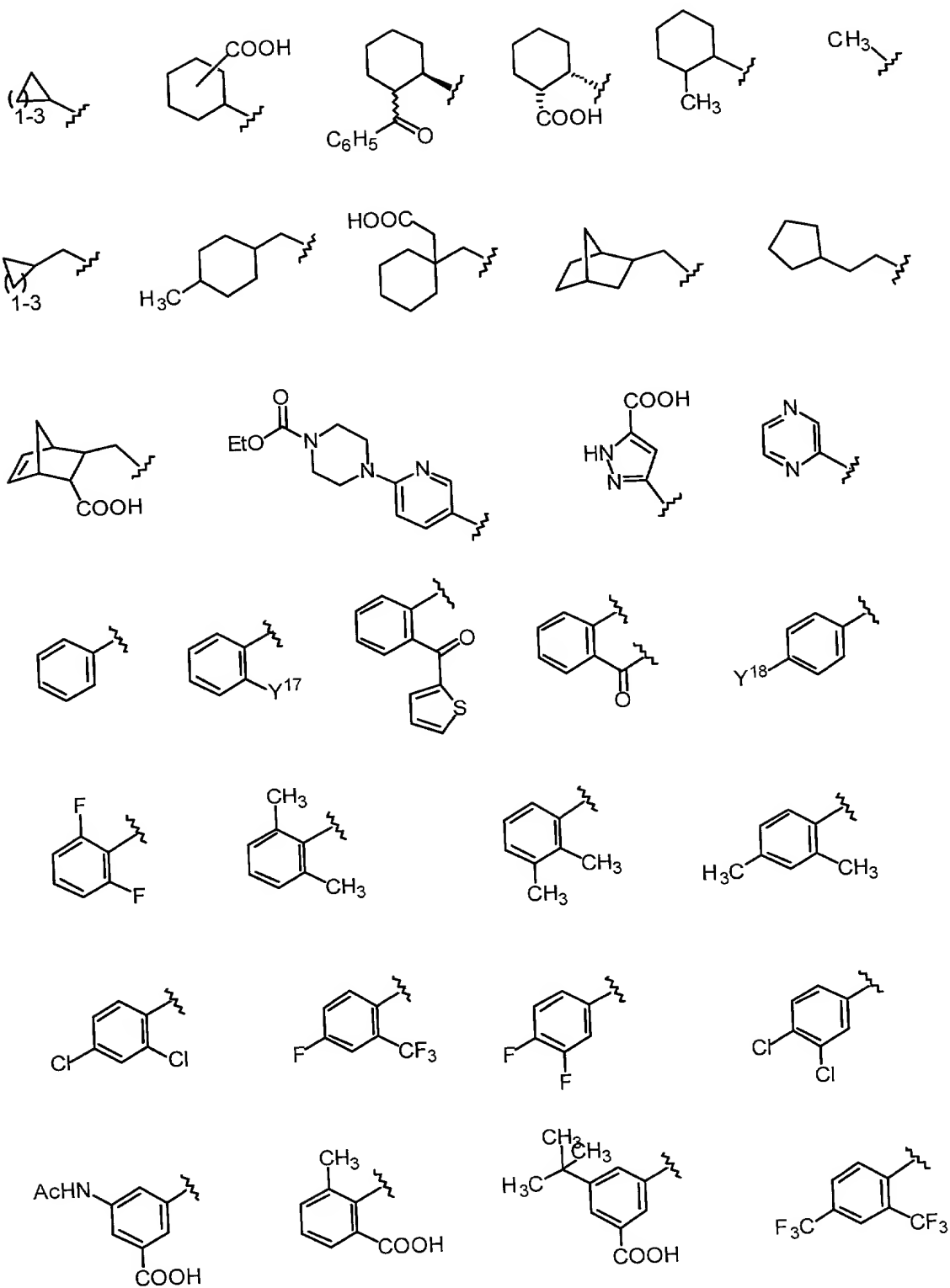
9. The compound of claim 8, wherein R^3 is selected from the following structures:

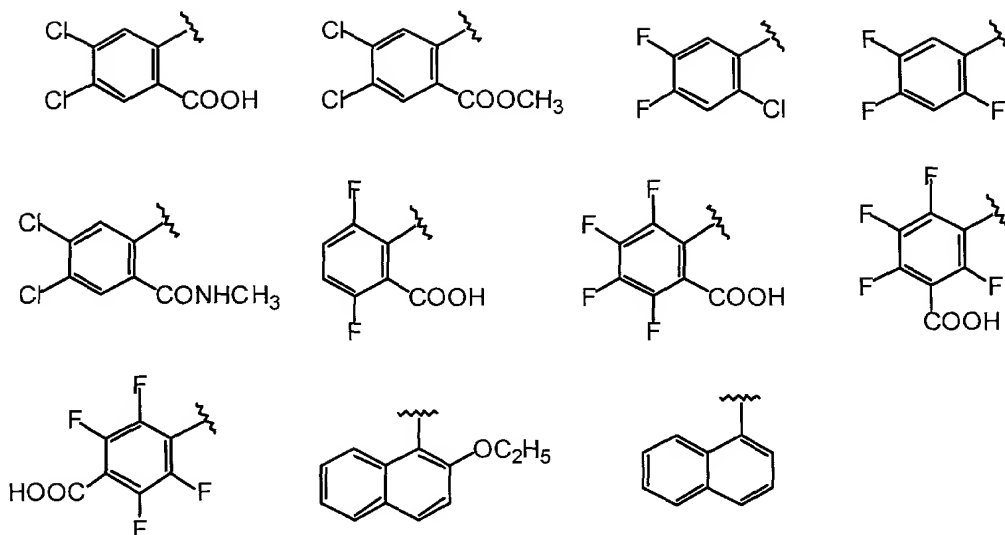


10. The compound of claim 9, wherein Z = N and R⁴ = H.
 11. A compound of claim 10, wherein W is C=O, or SO₂.
 12. A compound of claim 11, wherein Y is selected from the following
- 5 moieties:







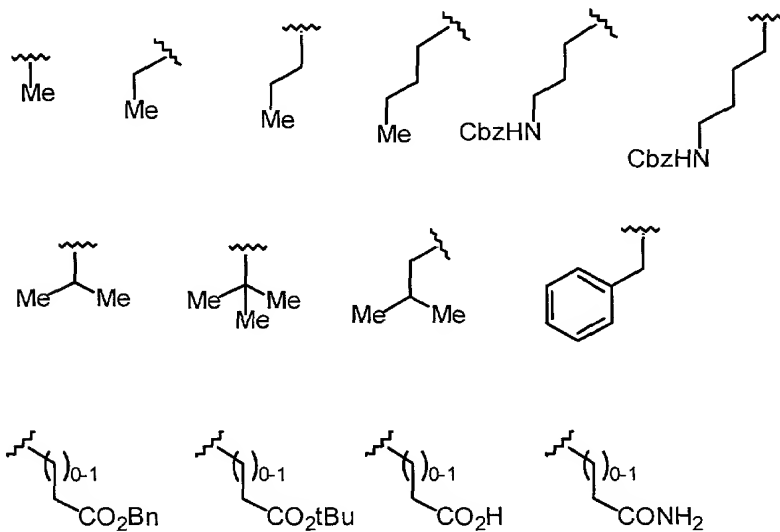


wherein:

Y^{11} is selected from H, COOH, COOEt, Ome, Ph, Oph, NHMe, NHAc, NHPH, CH(Me)₂, 1-triazolyl, 1-imidazolyl, and NHCH₂COOH;

Y^{12} is selected from H, COOH, COOMe, Ome, F, Cl, or Br;

Y^{13} is selected from the following moieties:



Y^{14} is selected from MeSO₂, Ac, Boc, ⁱBoc, Cbz, or Alloc;

Y^{15} and Y^{16} may be the same or different and are independently selected from alkyl, aryl or herereoalkyl, or heteroaryl;

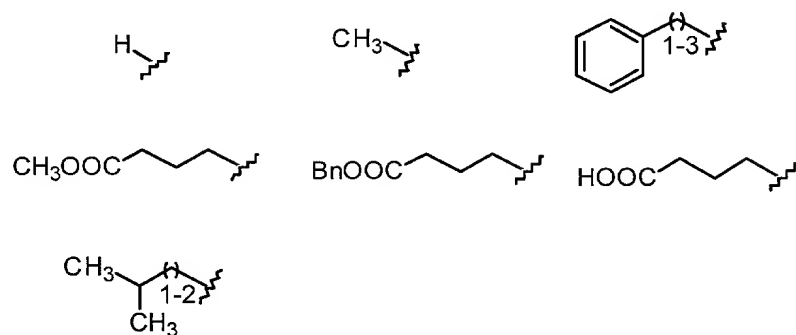
Y^{17} is CF_3 , NO_2 , $CONH_2$, OH , $COOCH_3$, OCH_3 , OC_6H_5 , C_6H_5 , COC_6H_5 , NH_2 , or $COOH$; and

5 Y^{18} is $COOCH_3$, NO_2 , $N(CH_3)_2$, F , OCH_3 , CH_2COOH , $COOH$, SO_2NH_2 , or $NHCOCH_3$.

13. A compound of claim 12, wherein Y is selected from the group consisting of:

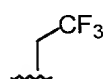
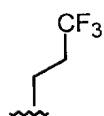
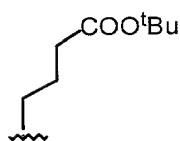
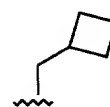
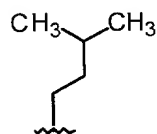
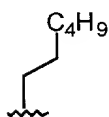
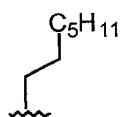
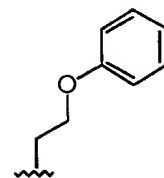
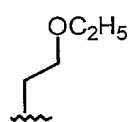
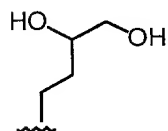
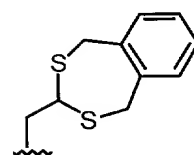
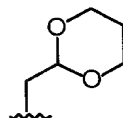
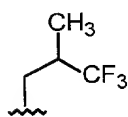
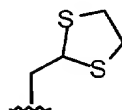
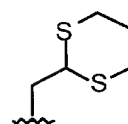
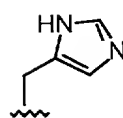
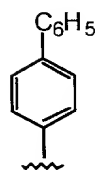
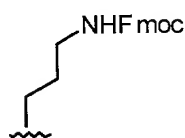
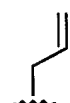
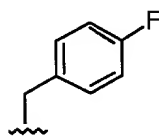
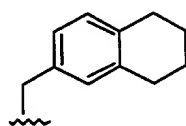
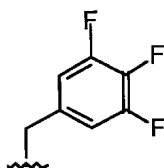
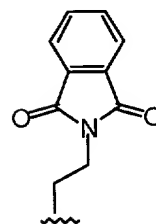
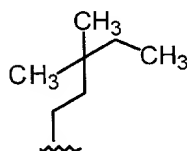
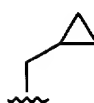
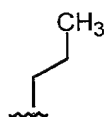
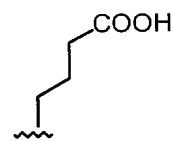
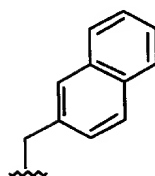
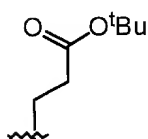
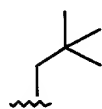
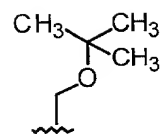
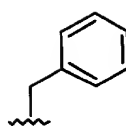
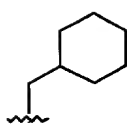
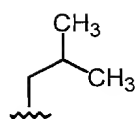

$$Y^{18} = F, COOH,$$

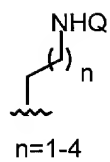
14. The compound of claim 13, wherein J is selected from the group consisting of:



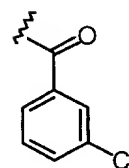
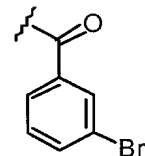
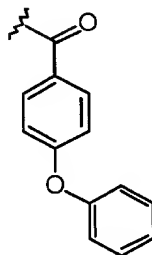
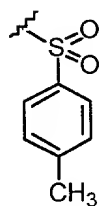
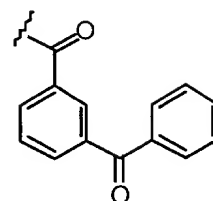
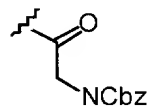
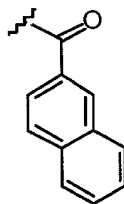
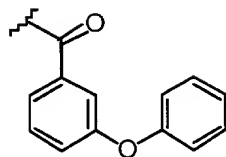
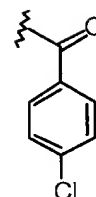
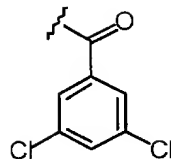
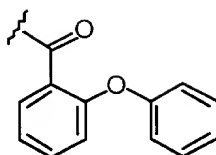
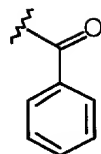
15. The compound of claim 14 where in J is H, CH₃ or Bn.

5 16. The compound of claim 15 wherein G is selected from moieties:



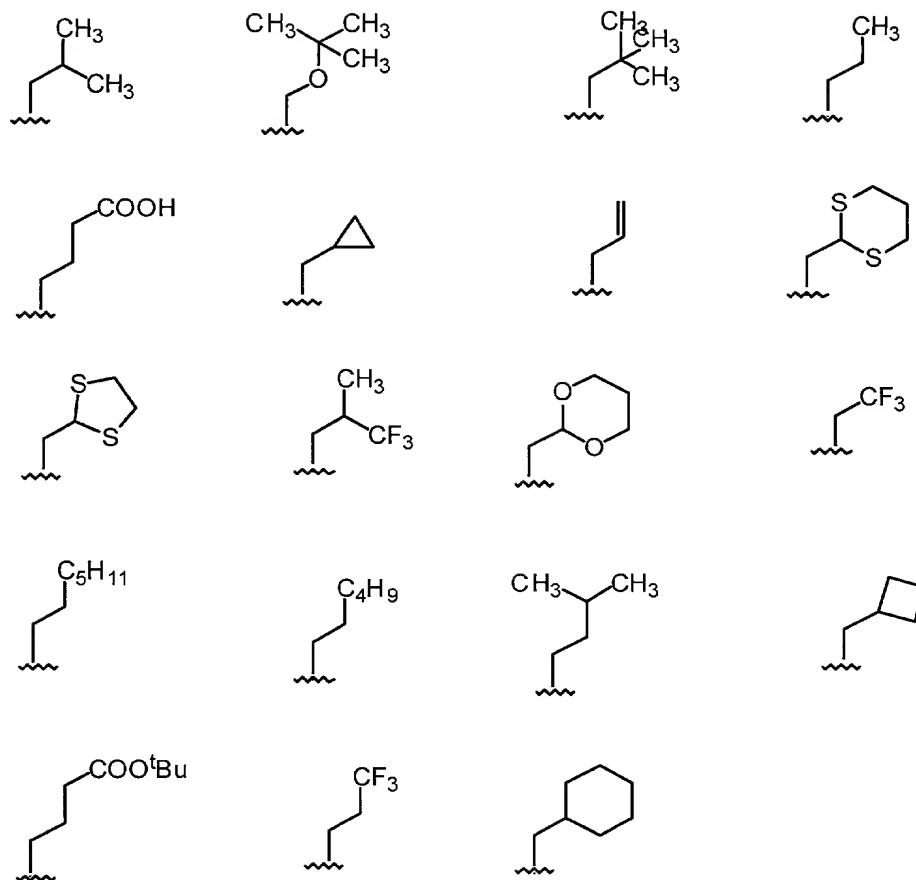


Q=



T05T20-2T050550

- 5 17. The compound of claim 16, wherein G is selected from the group consisting of :



18. A pharmaceutical composition comprising as an active ingredient a compound of claim 1.

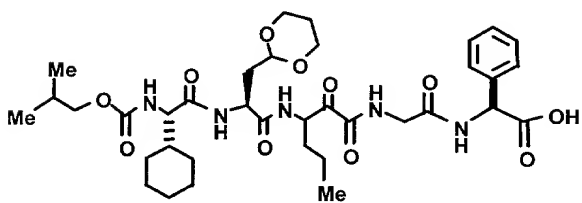
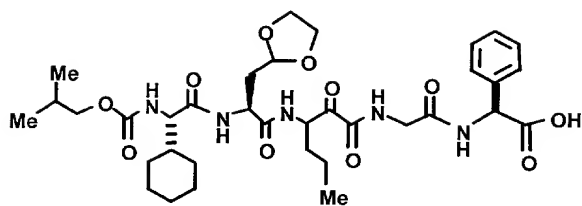
19. The pharmaceutical composition of claim 18 for use in treating disorders associated with Hepatitis C virus.

20. The pharmaceutical composition of claim 18 additionally comprising a pharmaceutically acceptable carrier.

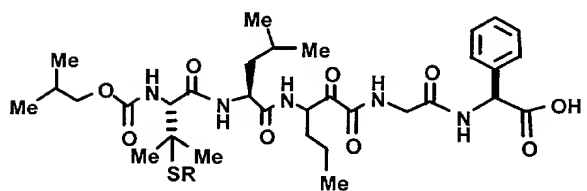
21. A method of treating disorders associated with the HCV protease, said method comprising administering to a patient in need of such treatment a pharmaceutical composition which composition comprises therapeutically effective amounts of a compound of claim 1.

22. The method of claim 21, wherein said administration is via subcutaneous administration.

23. The use of a compound of claim 1 for the manufacture of a medicament to treat disorders associated with the HCV protease.

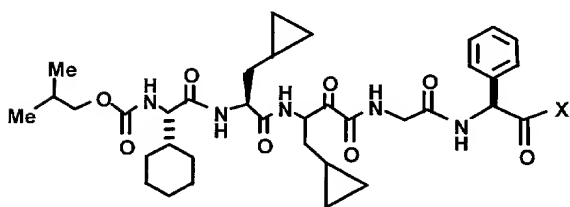


5



R = Me

R = Benzyl



10

X = O^tBu

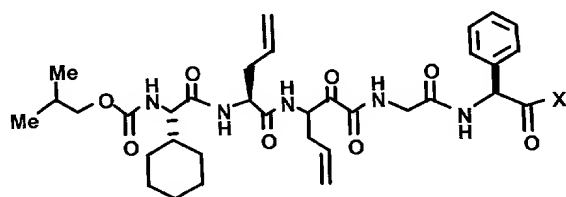
X = OH

X = NH₂

X = NMeOMe

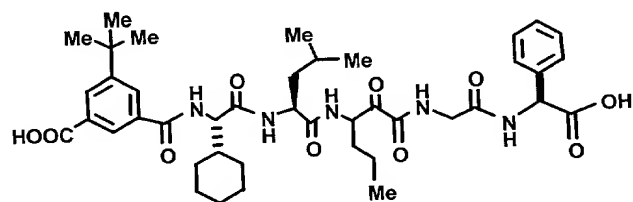
X = NMe₂

180

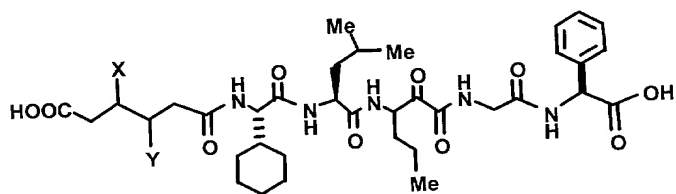


X = O^tBu

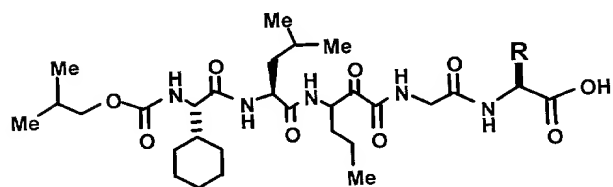
X = OH



5

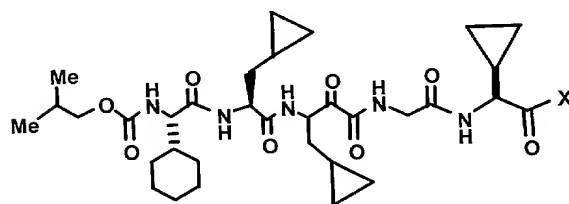


X = H, Y = tBu; X = tBu, Y = H



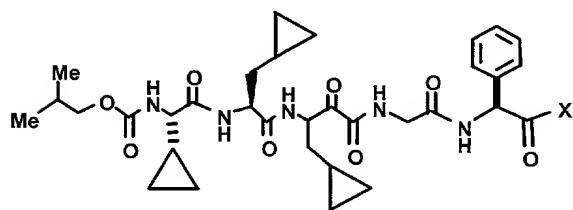
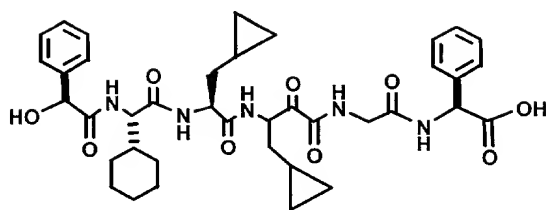
R = Propargyl; R = Allyl

10



X = O^tBu; X = OH

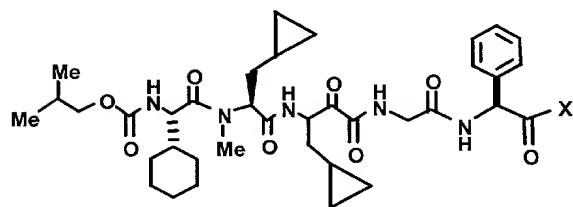
181



X = O^tButyl

X = OH

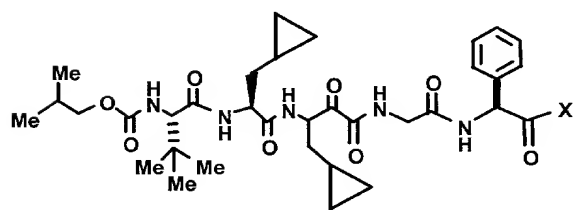
5



X = O^tButyl

X = OH

X = NMe₂

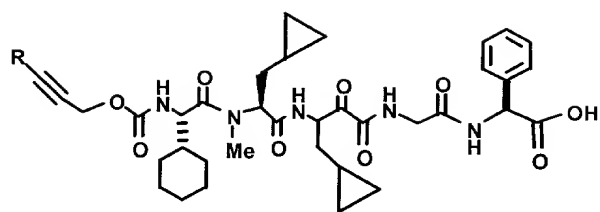


X = O^tBu

X = OH

10

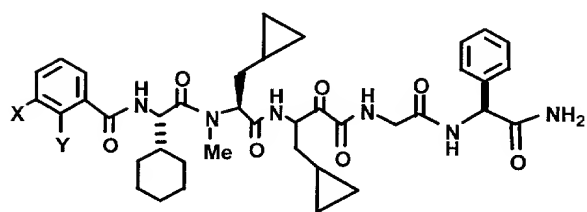
182



R = ^tBu

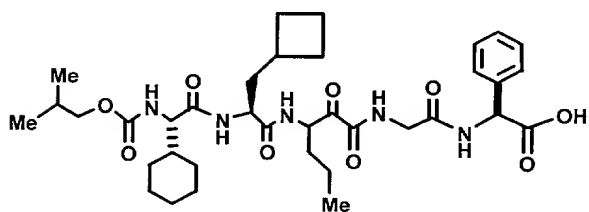
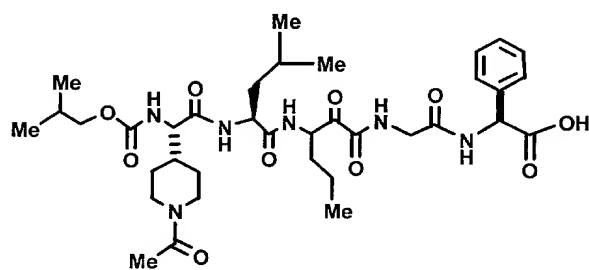
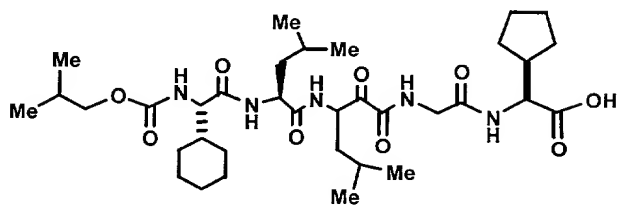
R = H

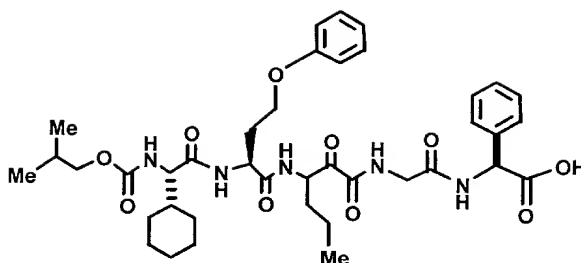
R = Me



X = H, Y = COOH

X = COOH, Y = H





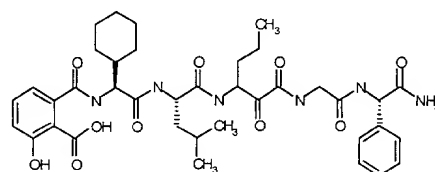
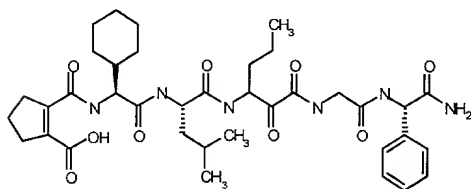
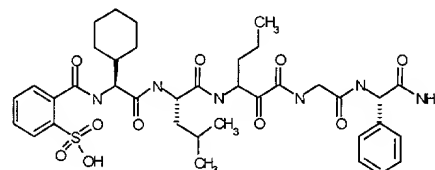
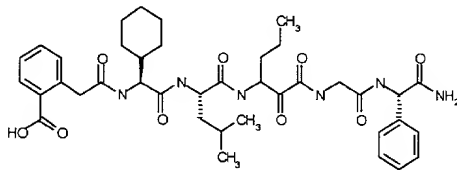
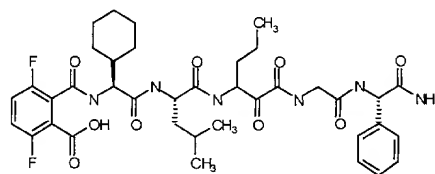
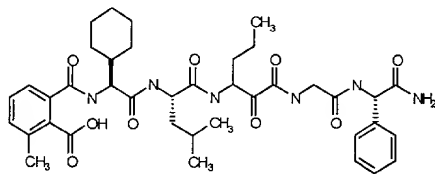
26. A pharmaceutical composition for treating disorders associated with the HCV protease, said composition comprising therapeutically effective amount
5 of one or more compounds in claim 25 and a pharmaceutically acceptable carrier.

27. The pharmaceutical composition of claim 26, additionally containing an antiviral agent.

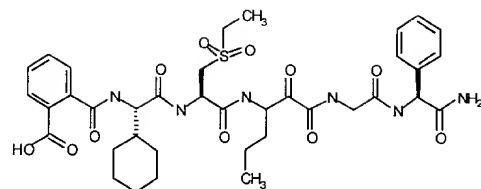
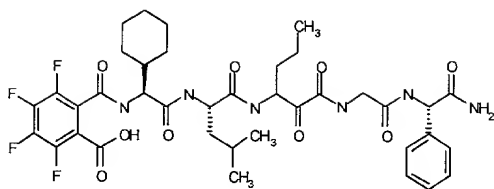
28. The pharmaceutical composition of claim 26 or claim 27, still
10 additionally containing an interferon.

29. The pharmaceutical composition of claim 28, wherein said antiviral agent is ribavirin and said interferon is α -interferon.

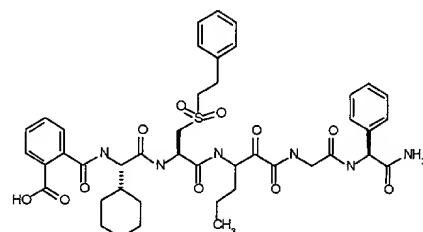
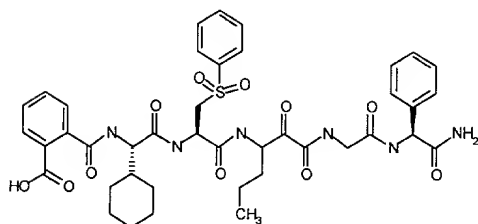
30. A compound selected from the group consisting of:



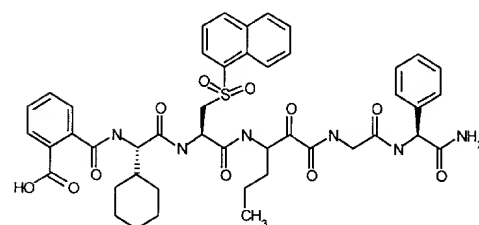
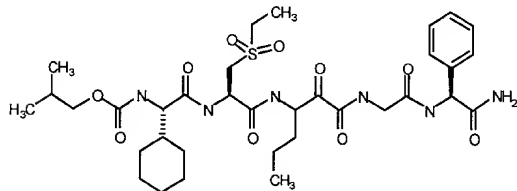
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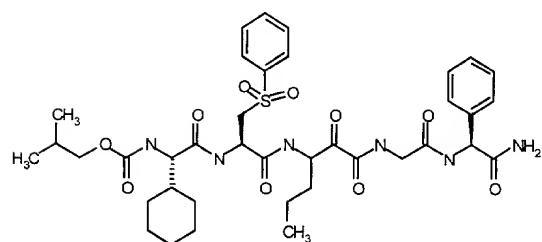
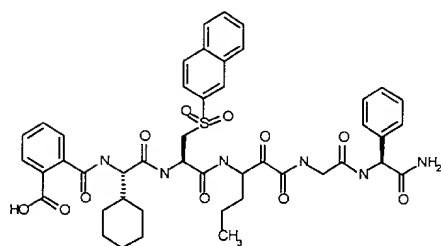
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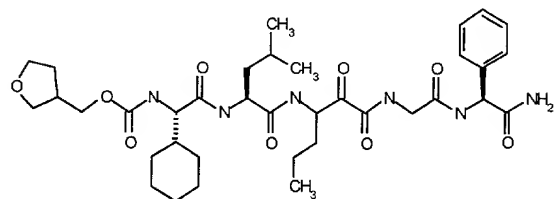
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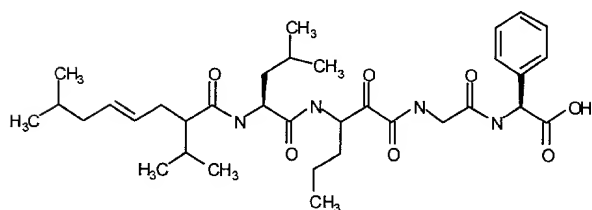


25



and

30



or an enantiomer, stereoisomer, rotamer or tautomer thereof, or a pharmaceutically acceptable salt or solvate thereof, wherein the compound exhibits HCV inhibitory activity.

5 31. A pharmaceutical composition, comprising one or more compounds of claim 30.

32. A method of treatment of an hepatitis C virus associated disorder, comprising administering an effective amount of one or more compounds of claim 30.

10 33. A method of modulating the activity of hepatitis C virus (HCV) protease, comprising contacting HCV protease with one or more compounds of claim 30.

34. A method of treating, preventing, or ameliorating one or more symptoms of hepatitis C, comprising administering an effective amount of one or more compounds of claim 30.

35. The method of claim 33, wherein the HCV protease is the NS3/NS4a protease.

36. The method of claim 35, wherein the compound or compounds inhibit HCV NS3/NS4a protease.

20 37. A method of modulating the processing of hepatitis C virus (HCV) polypeptide, comprising contacting a composition containing the HCV polypeptide under conditions in which the polypeptide is processed with one or more compounds of claim 30.

38. The compound of claim 7, wherein R³ is cyclohexyl.

25 39. The compound of claim 11, wherein Y is selected from the group consisting of 2-carboxy-3-hydroxyphenyl, 3-tetrahydrofurylmethoxy, and 2-sulfophenyl.

40. The compound of claim 15, wherein G is selected from the group consisting of ethylsulfonylmethyl, phenylsulfonylmethyl, 2-phenylethylsulfonylmethyl and 1-naphthylsulfonylmethyl.

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